

REMARKS

Claims 6-12 and 14 are pending in the application. Applicants retain the right to file a continuation and/or divisional application to any canceled claims. No new matter has been added.

The outstanding issues in this application are as follows:

- Claims 6-8, 10, 12, and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) in view of Williams et al. (5,171,989).
- Claims 9 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) and Williams et al. (5,171,989) as applied to claims 6-8, 10, 12 and 13 and further in view of Mian (6,319,469).

Applicants respectfully traverse the outstanding rejections, and Applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

I. 35 U.S.C. 103(a) as being unpatentable over Litborn in view of Williams et al.

Claims 6-8, 10, 12, and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) in view of Williams et al. (5,171,989). Applicants respectfully traverse this rejection.

Applicants remind the Examiner that when an obviousness determination is based on multiple prior art references, there must be a showing of some teaching, suggestion or reason to combine the references. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 53 USPQ2d 1580 (Fed. Cir. 2000). In this case, there is no suggestion to combine Litborn and Williams. Applicants assert that it is implausible that one skilled in the art would have the motivation, based on any suggestion in the references themselves, to apply information leading to a more reproducible ice formation in a mass spectrometer in a vacuum to solve an evaporation problem in an open reaction area of a microfluidic device related to keeping reactant concentrations constant and/or keeping the microvolume constant.

Applicants respectfully remind the Examiner that section 103 requires consideration of the claimed invention “as a whole.” This “as a whole” requirement prevents evaluation of the invention part by part, in hindsight. *Envtl. Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 698 (Fed. Cir. 1983). Without this requirement, an obviousness assessment could break an invention into its component parts, then find a prior art reference containing the component parts, and on that basis alone declare the invention obvious. It appears that the Examiner has indicated that Litborn disclosed a method of controlling evaporation and Williams discloses additions of solvents to aqueous sample. Thus, the Examiner believes that it is within the purview of one of skill in the art to combine these references to produce the present invention. Applicants contend that the Examiner is using improper hindsight to combine the references. The courts have refused to act on this type of hindsight reasoning, which uses the invention as a roadmap to find its prior art components. This type of analysis discounts the value of novel selection inventions. Thus, the courts have required that an Examiner must show some suggestion or motivation, excluding the invention itself, to make the new combination. See *In re Rouffet*, 149 F.3d 1350, 1355-56 (Fed. Cir. 1998); *In re Lee* 277 F. 2d 1338, 61 USPQ 2d 1430 (Fed. Cir. 2002); and *c.f. Ruiz v. A.B. Chance Co.*, F.3d 1270 (Fed. Cir. 2004).

Turning to the specifics of the pending Office Action, the Examiner has previously indicated that Litborn fails to teach the use of a cover liquid that is miscible with the sample liquid. In this Office Action, the Examiner has indicated that Williams does not address evaporation prevention and indicated that this was not necessary since Litborn addresses evaporation. Applicants remind the Examiner that the evaporation prevention taught in Litborn is diametrically opposite as to the claims of the present invention where evaporation is allowed, but the liquid volume disappearing by evaporation is replenished. Litborn requires an additional liquid, a covering liquid, that is immiscible with the sample liquid.

In response to Applicant’s request for the Examiner to specifically identify a suggestion to combine the references, the Examiner referred to two passages in Litborn. Firstly, the Examiner indicated that claim 9, page 9, lines 23-26 and 31-34 or claims 10 and 11 and page 9, lines 27-30 mentions “interact with reaction products” or “provide reagents.” Applicants assert that the Examiner has misconstrued these statements in Litborn. Firstly, claim 9 refers to a covering liquid that is substantially inert. As one of skill in the art is

aware, the term inert refers to liquids not active or not reactive. Thus, claim 9 does not suggest “mixing of the solvent and sample.”

Claim 10 and page 9, lines 23-26 of Litborn mentions that it would be interesting to use a cover liquid which interacts with reaction products, e.g., waste products from the sample. Applicants assert that this still does not provide a suggestion that the covering liquid is miscible with the underlying sample liquid. The solvent and covering liquid of Litborn are not the same. Still further, the mention of reaction products would indicate that the reaction has been performed. Applicants remind the Examiner that the key feature of Litborn is two liquids that are immiscible. The first liquid is the underlying sample liquid and the second liquid is the covering liquid that prevents evaporation. Thus, claim 10 and page 9, lines 23-26 does not suggest “mixing of the solvent and sample.”

Claim 11 and page 9, lines 27-30 of Litborn mentions that in other cases it can be of value to include one or more reactants to be used in the operation in the covering liquid. This still does not provide a suggestion that the covering liquid is miscible with the sample liquid. This merely mentions that reactants may be present in the covering liquid, but nothing about mixing or miscibility of the two liquids. The key feature of Litborn is two liquids that are immiscible. The first liquid is the sample liquid and the second liquid is the covering liquid that prevents evaporation. The covering liquid has a certain density so that it floats on top of the sample liquid. One of skill in the art would assume the cited passage to mean that reactants that are present in the covering liquid gradually would partition to the sample liquid where the reaction takes place. Thus, claim 11 and page 9, lines 27-30 does not suggest “mixing of the two liquids.”

Page 9, lines 31-34 of Litborn mentions the case where the covering liquid is chosen to have the ability of extracting one or more components from the sample. This still does not provide a suggestion that the covering liquid is miscible with the sample liquid. If this part of Litborn would suggest miscibility of the two liquids with each other it would also suggest an enhanced risk for evaporation of the sample liquid.

In view of the above, Applicants assert that one of skill in the art would not interpret these passages of Litborn to provide a suggestion of using a replenishing solvent that is miscible with a sample liquid as in the pending claims.

Williams et al. disclose the method of adding a miscible solvent to a capillary leading liquid sample to the vacuum chamber of a mass spectrometer in order to reduce the freezing point of the liquid entering the vacuum chamber via the capillary, thereby improving the reproducibility in ice formation at the capillary end. Applicant respectfully points out that Williams et al. do not teach addition of a miscible solvent to prevent evaporation at the capillary end, nor replacing such solvent. Williams et al. do not teach performing reactions at the end of the capillary with reactants that must be present in accurate concentrations in order to reach reproducible results. The Examiner has continued to assert that Williams teaches a sample loading method in which the sample is mixed with a miscible solvent for the purpose of changing a property of the sample mixture. Still further, the Examiner has indicated that he believes one of skill in the art would look at the addition of a miscible solvent to the sample in Williams as a way to provide the “interaction” suggested in a variant of Litborn where immiscibility still is a key feature. The Examiner is reminded that the main focus of Litborn is the use of a covering liquid that is immiscible with the underlying sample liquid from which evaporation is to be prevented. One of skill in the art would not be motivated to combine the teachings of Litborn with that of Williams. If the two references were combined, then the method of preventing evaporation of Litborn would not function the way intended by Litborn, in fact, there would be an enhanced risk for evaporation of the sample liquid compared to the variant in which the two liquids are immiscible.

Applicants note that as indicated in MPEP 2144.03 and in keeping with *In re Zurko* (258 F.3d 1385, 59 USPQ2d 1697 (Fed. Cir. 2001)), an assessment of basic knowledge and common sense that is not based on any evidence in the record lacks substantial evidence support, and the Examiner has provided no evidentiary support for the assertion that one of skill in the art would combine Litborn with Williams to obtain Applicant’s invention. The Examiner must provide specific factual findings predicated on sound technical and scientific reasoning to support his or her conclusion of common knowledge. *In re Chevenard*, 139 F.2d 713, 60 USPQ 241 (CCPA 1943). *In re Soli*, 317 F. 2d 941, 945-946, 137 USPQ 797, 800 (CCPA 1963). Moreover, if the Applicant adequately traverses the Examiner’s assertion of

official notice, the Examiner must provide documentary evidence in the next Office Action if the rejection is to be maintained. See 37 CFR §1.104 (c)(2) and *Zurko*, 258 F.3d at 1386, 59 USPQ2d at 1697. If the Examiner is relying on personal knowledge to support the finding of what is known in the art, the Examiner must provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. See 37 CFR §1.104(d)(2).

In view of the above arguments, Applicants assert that the claims are non-obvious and request that the rejection be withdrawn.

II. 35 U.S.C. 103(a) as being unpatentable over Litborn and Williams et al., and further in view of Mian (6,319,469).

Claims 9 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) and Williams et al. (5,171,989) as applied to claims 6-8, 10, 12 and 13 and further in view of Mian (6,319,469). Applicants respectfully traverse this rejection.

As discussed previously, Litborn does not teach the use of a cover liquid that is miscible with the sample liquid and Williams et al. do not teach addition of a miscible solvent to prevent evaporation at the capillary end, nor replacing such solvent, nor doing so in an open microarea. Therefore, Litborn in combination with Williams et al. does not render obvious claims 9 or 11, for the same reasons previously discussed. As stated by the Examiner in the previous office action, Mian (6,319,469) discloses a microfluidic device used to analyze microsamples, however, Mian does not teach evaporation control. More specifically, Mian does not teach the use of a covering liquid to aid in preventing evaporation, or replenishing of liquid that has evaporated. Rather, Mian discloses the use of microchannels in a disk that is rotated to utilize centripetal forces to move samples in the microchannels. The invention disclosed by Mian could not even permit replenishment of liquid that has evaporated, as there is no prolonged fluid connection between the pipette barrels or hollow tubes and the inlet ports of the microfluidic device disclosed by Mian. The Examiner has failed to show, as required, that all the claimed limitations are taught or suggested by the cited references.

Furthermore, as has been previously discussed, there must be a showing of some teaching, suggestion or reason to combine the references when an obviousness determination

is based on multiple prior art references. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 53 USPQ2d 1580 (Fed. Cir. 2000). In this case, there is no suggestion to combine Litborn and Williams, nor Litborn and Mian, nor a combination of the three. Applicants assert that it is implausible that one skilled in the art would have the motivation, based on any suggestion in the references themselves, to combine a) a first reference that discloses preventing evaporation from a sample liquid by the use of a liquid that is immiscible with the sample liquid, with b) a second reference that does not deal with preventing evaporation and discloses the use of liquid that contrary to the first reference is miscible with the sample liquid, to result in the claimed invention. Applicants respectfully point out that the Examiner has not discussed or identified any requisite suggestion to combine the references, but merely said that one would do so by reading into the references matters that are not present therein. Applicants remind the Examiner that as required by the substantial evidence rule, if the Examiner continues to maintain that Litborn, Williams et al., and Mian suggest their combination, the Examiner is requested to make of record the passage relied upon, or state for the record that no such teaching can be found in these references. See, *In re Gartside*, 203 F.3d 1305, 53 USPQ2d 1769 (Fed. Cir. 2000).

In view of the above arguments, Applicants assert that the claims are non-obvious and respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02149US0 from which the undersigned is authorized to draw.

Dated: July 5, 2005

Respectfully submitted,

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